

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents





Letter to the Editor

Response to effect estimation of hydroxychloroquine for COVID-19: a secondary analysis of an open label non-randomized clinical trial.



We agree with colleagues that in our first paper, some estimate measures of effect modification such as relative risk reduction (RRR), absolute risk reduction (ARR) and number needed to treat (NNT) with the intervention of hydroxychloroquine were not analyzed [1]. In addition, excluding six patients from our analysis may have biased our results.

For that reason, we reanalyzed our data about all 42 patients initially enrolled in our survey. Outcome of analysis was "contagiousness at day 7". According to WHO criteria, patients were considered not contagious if they have two consecutive negative PCR results at least 24 hours apart [2]. Analysis was carried out using the STATA version 15.1 statistical package.

Table 1 shows the contingency table and the estimated effect measures. The incidence of the hydroxychloroquine (HCQ) exposed group was 0.5 and the incidence of the unexposed group was 0.1667. The treatment with HCQ increased by a factor of 2 the proportion of non-contagious patients at day 7 (relative risk (RR) = 1.80, 95%CI = [1.10 - 2.94], p = 0.0257). The RRR was 2.0, the ARR was 0.36, 95%CI = [0.08 - 0.63] and NNT was 2.81, 95%CI = [1.58 - 12.55]. HCQ and azithromycin (AZ) combined treatment increased by a factor of 4 the proportion of noncontagious patients at day 7 (RR = 3.75, 95%CI = [1.17 - 12.01], 0.0194. The RRR was 2.75, the ARR was 0.45, 95%CI = [0.08 - 0.84]and NNT was 2.18, 95%CI = [1.20 - 12.30].

In conclusion, the reintegration of excluded patients in our analysis and the calculation of the estimate measures of effect modification confirm the effectiveness of the HCQ alone and of HCQ-AZ treatments on viral clearance of SARS-CoV-2 in COVID-19 patients.

Table 1 Hydroxychloroquine and COVID-16 negative PCR

	Contagiousness at Day7	
	Event (negative PCR)	No event (positive PCR)
Hydroxychloroquine versus contro	1	
Case (HCQ)	12	12
Control	3	15
Relative risk [95%CI], p-value	1.80 [1.10 - 2.94], p = 0.0257	
Relative risk reduction	2.0	
Absolute risk reduction [95%CI]	0.36 [0.08 - 0.63]	
Number needed to treat [95%CI]	2.81 [1.58 - 12.55]	
Hydroxychloroquine and azithrom	ycin combined treatme	nt versus control
Case $(HCQ + AZ)$	5 3	
Control	3 15	
Relative risk [95%CI], p-value	3.75 [1.17 - 12.01], 0.0194	
Relative risk reduction	2.75	
Absolute risk reduction [95%CI]	0.45 [0.08 - 0.84]	
Number needed to treat [95%CI]	2.18 [1.20 - 12.30]	

[☆] This article 10.1016/j.ijantimicag.2020.106172.

10.1016/j.ijantimicag.2020.105949 10.1016/j.ijantimicag.2020.106172,

DOIs of original articles:

10.1016/j.ijantimicag,2020.105949

Funding

No funding sources

Competing interest

The authors declare no competing interests.

Ethical approval

Not applicable

References

- [1] Martinez-Arboleda JJ, Isaza-Pierotti DF, Rosso FIJAA-D-20-00548 Parra-Lara LG. Effect estimation of hydroxychloroquine for COVID-19: a secondary analysis of an open label non-randomized clinical trial. Int J Antimicrob Agents 2021:106172.
- [2] European Centre for Disease Prevention and Control. Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 first update. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-guidance-discharge-and-ending-isolation-first% 20update.pdf (Accessed 4 October, 2020)

Philippe Gautret IHU-Méditerranée Infection, Marseille, France

Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France

Van Thuan Hoang

IHU-Méditerranée Infection, Marseille, France Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France Thai Binh University of Medicine and Pharmacy, Thai Binh, Vietnam

> Jean-Christophe Lagier, Didier Raoult* IHU-Méditerranée Infection, Marseille, France Aix Marseille Univ, IRD, APHM, MEPHI, Marseille, France

*Corresponding author: Didier Raoult. E-mail address: Didier.raoult@gmail.com (D. Raoult)